| | Type | L # | Hits | Search Text | DBs | Time Stamp | Comments | Error Definition | Errors |
|---|---|---|---|---|---|---|---|---|---|
| 11 | BRS | L12 | 2 | 3 same 11 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/07/16 12:05 | | | 0 |
| 12 | BRS | L13 | 26581 | ( metabolic adj disorder) or (glucose adj tolerance) or (diabetes adj mellitus) or neuropathy | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/07/16 12:07 | | | 0 |
| 13 | BRS | L14 | 75 | 13 same 1 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/07/16 12:08 | | | 0 |
| 14 | BRS | L15 | 3 | 13 same 1 same masked | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/07/16 12:08 | | | 0 |
| 15 | BRS | L16 | 0 | 14 same 5 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/07/16 12:09 | | | 0 |

| | Type | L # | Hits | Search Text | DBs | Time Stamp | Comments | Error Definition | Errors |
|---|---|---|---|---|---|---|---|---|---|
| 1 | BRS | L1 | 488 | (dipeptidyl adj peptidase adj IV) or (DP adj IV) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/07/16 11:34 | | | 0 |
| 2 | BRS | L3 | 317 | 1 same inhibit$3 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/07/16 11:36 | | | 0 |
| 3 | BRS | L4 | 3 | 3 same masked | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/07/16 11:45 | | | 0 |
| 4 | BRS | L5 | 47447 | (alkyl adj ketone) or (chloroalkyl adj ketone) or cyanide | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/07/16 11:59 | | | 0 |
| 5 | BRS | L6 | 1 | 3 same 5 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/07/16 11:58 | | | 0 |
| 6 | BRS | L7 | 0 | (dipeptide adj alkyl adj ketone) or (dipeptide adj chloroalkyl adj ketone) or (dipeptide adj cyanide) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/07/16 12:01 | | | 0 |
| 7 | BRS | L8 | 1 | (peptide adj alkyl adj ketone) or (peptide adj chloroalkyl adj ketone) or (peptide adj cyanide) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/07/16 12:02 | | | 0 |
| 8 | BRS | L9 | 4 | (peptidyl adj alkyl adj ketone) or (peptidyl adj chloroalkyl adj ketone) or (peptiddyl adj cyanide) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/07/16 12:02 | | | 0 |
| 9 | BRS | L10 | 0 | 9 same 1 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/07/16 12:03 | | | 0 |
| 10 | BRS | L11 | 6 | (Ile-thia) or (ile-pyr) or (val-thia) or (val-pyr) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2003/07/16 12:04 | | | 0 |

```
FILE 'MEDLINE' ENTERED AT 12:16:[redacted] ON 16 JUL 2003

FILE 'CAPLUS' ENTERED AT 12:16:08 ON 16 JUL 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'BIOSIS' ENTERED AT 12:16:08 ON 16 JUL 2003
COPYRIGHT (C) 2003 BIOLOGICAL ABSTRACTS INC.(R)

FILE 'EMBASE' ENTERED AT 12:16:08 ON 16 JUL 2003
COPYRIGHT (C) 2003 Elsevier Science B.V.  All rights reserved.

FILE 'SCISEARCH' ENTERED AT 12:16:08 ON 16 JUL 2003
COPYRIGHT 2003 THOMSON ISI

FILE 'AGRICOLA' ENTERED AT 12:16:08 ON 16 JUL 2003

=> s (DP IV) or (dipeptidyl peptidase iv)
L1        6267 (DP IV) OR (DIPEPTIDYL PEPTIDASE IV)

=> s l1 (p) inhibt?
L2           0 L1 (P) INHIBT?

=> s l1 (p) inhibit?
L3        1882 L1 (P) INHIBIT?

=> s l3 (p) masked
L4           2 L3 (P) MASKED

=> duplicate remove l4
DUPLICATE PREFERENCE IS 'CAPLUS, EMBASE'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L4
L5           1 DUPLICATE REMOVE L4 (1 DUPLICATE REMOVED)

=> d l5 1 ibib abs

L5   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2003 ACS         DUPLICATE 1
ACCESSION NUMBER:         1982:522831  CAPLUS
DOCUMENT NUMBER:          97:122831
TITLE:                    Dipeptidyl peptidase IV inhibits the polymerization of
                          fibrin monomers
AUTHOR(S):                Mentlein, Rolf; Heymann, Eberhard
CORPORATE SOURCE:         Med. Fak., Univ. Kiel, Kiel, D-2300, Fed. Rep. Ger.
SOURCE:                   Archives of Biochemistry and Biophysics (1982),
                          217(2), 748-50
                          CODEN: ABBIA4; ISSN: 0003-9861
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   A highly purified   ***dipeptidyl***     ***peptidase***     ***IV***
     (I) from human placenta cleaved glycylproline from the N-terminal end of
     the fibrin .alpha. chain and   ***inhibited***   the clotting of fibrin
     monomers.  This result underlined the importance of the N-terminus of the
     fibrin .alpha. chain as an aggregation site   ***masked***   by
     fibrinopeptide A.  Apparently, I can hinder blood coagulation in intact
     vessels in vivo, because it is located on the surface of the capillary
     endothelium.


=> d his

     (FILE 'HOME' ENTERED AT 12:15:44 ON 16 JUL 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     12:16:08 ON 16 JUL 2003
L1        6267 S (DP IV) OR (DIPEPTIDYL PEPTIDASE IV)
L2           0 S L1 (P) INHIBT?
L3        1882 S L1 (P) INHIBIT?
L4           2 S L3 (P) MASKED
L5           1 DUPLICATE REMOVE L4 (1 DUPLICATE REMOVED)

=> s l3 (p) unstable
L6          12 L3 (P) UNSTABLE

=> duplicate remove l6
```

DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN [redacted] FILE? Y/(N):n
PROCESSING COMPLETED FOR L6
L7 4 DUPLICATE REMOVE L6 (8 DUPLICATES REMOVED)

=> d l7 1-4 ibib abs

L7 ANSWER 1 OF 4 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2001410442 MEDLINE
DOCUMENT NUMBER: 21235368 PubMed ID: 11337057
TITLE: Transbuccal peptide delivery: stability and in vitro permeation studies on endomorphin-1.
AUTHOR: Bird A P; Faltinek J R; Shojaei A H
CORPORATE SOURCE: Department of Pharmaceutical Sciences, School of Pharmacy, Texas Tech University Health Sciences Center, Amarillo, TX 79106, USA.
SOURCE: JOURNAL OF CONTROLLED RELEASE, (2001 May 18) 73 (1) 31-6. Journal code: 8607908. ISSN: 0168-3659.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010723
Last Updated on STN: 20010723
Entered Medline: 20010719

AB The purpose of this study was to investigate the feasibility of buccal delivery of a model peptide, endomorphin-1 (ENI), using stability and in vitro permeation studies. ENI is a recently isolated mu-opiate receptor agonist with high selectivity and specificity for this receptor subtype. Stability studies were conducted in various buffers and the drug was shown to be stable in both acidic and basic buffer systems. In the presence of full thickness porcine buccal epithelium, ENI was ***unstable*** with only 23.4+/-15.7% intact drug present after 6 h. The region responsible for this degradation was found to coincide with the major barrier region of the buccal epithelium as delineated through stability experiments in the presence of partial thickness buccal epithelium. Various peptidase ***inhibitors*** were used to isolate the enzyme(s) responsible for this degradation. Diprotin-A, a potent ***inhibitor*** of ***dipeptidyl*** ***peptidase*** ***IV*** , provided significant ***inhibition*** of the degradation of ENI in the presence of buccal epithelium. In vitro permeation studies revealed that the permeability coefficient of ENI across porcine buccal epithelium was 5.67+/-4.74x10(-7) cm/s. The enzymatic degradation of ENI was found not to be rate limiting to the drug's permeation across buccal epithelium, as diprotin-A did not increase the permeation of ENI. Sodium glycocholate as well as sodium taurocholate were also ineffective in enhancing the permeation of ENI across porcine buccal epithelium.

L7 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:819402 CAPLUS
DOCUMENT NUMBER: 132:36038
TITLE: Synthesis of prodrugs of ***unstable*** ***dipeptidyl*** ***peptidase*** ***IV*** ***inhibitors*** for use in treating diabetes
INVENTOR(S): Demuth, Hans-Ulrich; Schmidt, Jorn; Hoffmann, Torsten; Glund, Konrad
PATENT ASSIGNEE(S): Probiodrug Gesellschaft Fur Arzneimittelforschung m.b.H., Germany
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9967279 | A1 | 19991229 | WO 1999-EP4381 | 19990624 |

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,

CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

| | | | | | |
|---|---|---|---|---|---|
| DE 19828114 | A1 | 200[redacted]27 | DE 1998-19828114 | 1998[redacted]24 |
| CA 2335978 | AA | 1999[redacted]229 | CA 1999-2335978 | 1999[redacted]24 |
| AU 9947772 | A1 | 20000110 | AU 1999-47772 | 19990624 |
| AU 758843 | B2 | 20030403 | | |
| BR 9911415 | A | 20010320 | BR 1999-11415 | 19990624 |
| EP 1090030 | A1 | 20010411 | EP 1999-931163 | 19990624 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2002518518 | T2 | 20020625 | JP 2000-555930 | 19990624 |
| NO 2000006483 | A | 20001219 | NO 2000-6483 | 20001219 |
| US 2001020006 | A1 | 20010906 | US 2000-745883 | 20001221 |

PRIORITY APPLN. INFO.: DE 1998-19828114 A 19980624
WO 1999-EP4381 W 19990624

OTHER SOURCE(S): MARPAT 132:36038
GI

/ Structure 1 in file .gra /

AB The invention relates to compds. of ***unstable*** ***inhibitors*** of ***dipeptidyl*** ***peptidase*** ***IV*** ( ***DP*** ***IV*** ) which comprise general formula A-B-C, whereby A represents an amino acid, B represents the chem. bond between A and C or an amino acid, and C represents an ***unstable*** ***inhibitor*** of ***DP*** ***IV*** . Such compds. are used for treating altered glucose tolerance, glucosuria, hyperlipidemia, metabolic acidosis, diabetes mellitus, diabetic neuropathy, nephropathy, and secondary diseases in mammals caused by diabetes mellitus. Thus, (I) was reacted with pyridine to give [(II); R = Cbz], which was deprotected to give II (R = H)(III) which is thought to undergo an intramol. cyclization (no data) to form the active ***DP*** ***IV*** ***inhibitor*** . In 0.1 M HEPES-buffer, pH 7.6, at 25.degree., III had a half life (before self-cyclization) of 13.3 min.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 4 MEDLINE DUPLICATE 2

ACCESSION NUMBER: 1998327123 MEDLINE
DOCUMENT NUMBER: 98327123 PubMed ID: 9660870
TITLE: Functional specialization of stable and dynamic microtubules in protein traffic in WIF-B cells.
AUTHOR: Pous C; Chabin K; Drechou A; Barbot L; Phung-Koskas T; Settegrana C; Bourguet-Kondracki M L; Maurice M; Cassio D; Guyot M; Durand G
CORPORATE SOURCE: Laboratoire de Biochimie Generale, Equipe d'Accueil 1595, Unite de Formation et de Recherche de Pharmacie, Universite Paris-Sud, 92296 Chatenay-Malabry, France.
SOURCE: JOURNAL OF CELL BIOLOGY, (1998 Jul 13) 142 (1) 153-65. Journal code: 0375356. ISSN: 0021-9525.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199808
ENTRY DATE: Entered STN: 19980828
Last Updated on STN: 19980828
Entered Medline: 19980820

AB We found that the magnesium salt of ilimaquinone, named 201-F, specifically disassembled dynamically ***unstable*** microtubules in fibroblasts and various epithelial cell lines. Unlike classical tubulin-interacting drugs such as nocodazole or colchicine which affect all classes of microtubules, 201-F did not depolymerize stable microtubules. In WIF-B-polarized hepatic cells, 201-F disrupted the Golgi complex and ***inhibited*** albumin and alpha1-antitrypsin secretion to the same extent as nocodazole. By contrast, 201-F did not impair the transport of membrane proteins to the basolateral surface, which was only affected by the total disassembly of cellular microtubules. Transcytosis of two apical membrane proteins-the alkaline phosphodiesterase B10 and ***dipeptidyl*** ***peptidase*** ***IV*** -was affected to the same extent by 201-F and nocodazole. Taken together, these results indicate that only dynamically ***unstable*** microtubules are involved in the transport of secretory proteins to the plasma membrane, and in the transcytosis of membrane proteins to the apical surface. By contrast, stable microtubules, which are not functionally affected by 201-F treatment, are involved in the transport of membrane proteins to the

basolateral surface. By specifically disassembling highly dynamic microtubules, 201-F is an [redacted]aluable tool with which to st[redacted] the functional specialization of stable and dynamic microtubules in living cells.

L7 ANSWER 4 OF 4 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95220827 EMBASE
DOCUMENT NUMBER: 1995220827
TITLE: Amino acid and peptide phosphonate derivatives as specific inhibitors of serine peptidases.
AUTHOR: Oleksyszyn J.; Powers J.C.
CORPORATE SOURCE: OsteoArthritis Sciences, Inc.,Cambridge, MA 02139, United States
SOURCE: Methods in Enzymology, (1994) 244/- (423-441).
ISSN: 0076-6879 CODEN: MENZAU
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Peptidyl derivatives of .alpha.-aminoalkyl phosphonate diphenyl esters have a number of advantages for in vitro and in vivo experiments compared to other commonly used peptide serine peptidase ***inhibitors*** . They are easily synthesized, are chemically very stable, and are not alkylating agents such as the commonly used peptide chloromethyl ketone serine peptidase ***inhibitors*** . They are more stable than most other organophosphorus ***inhibitors*** , including peptidyl derivatives of the .alpha.-aminoalkyl phosphonates, where the phosphonate moiety is chemically activated by the presence of better leaving groups. The .alpha.-aminoalkyl phosphonate diphenyl esters have outstanding stability (t(1/2) usually greater than 4 days at pH 7.5; >24 hr in plasma). Thus, low ***inhibitor*** concentrations can effectively control unwanted serine peptidase activity with low ***inhibitor*** concentrations over long time periods, which makes them perfect tools for experiments involving cells. Because .alpha.-aminoalkyl phosphonate diphenyl esters are irreversible ***inhibitors*** , they offer real advantages in many experimental situations over reversible ***inhibitors*** in cases in which it may be necessary to maintain high concentrations of the reversible ***inhibitor*** for long time periods. The second-order ***inhibition*** rate constants for phosphonate ***inhibitors*** are usually not as high as those observed with other types of peptidyl serine peptidase ***inhibitors*** . This is compensated for by their high stability and specificity. The irreversible character of the ***inhibition*** reaction allows effective ***inhibition*** even if the inactivation rate constant is not large. For example, Cbz-Val(P)(OPh)2 ***inhibits*** HLE with a rate constant of 260 M-1 sec-1. Thus at an effective concentration of 10 .mu.M, 50% of the enzyme is inactivated after 4.5 min, and almost no activity is detected after an 11-min incubation time. Frequently there is a need to specifically ***inhibit*** serine peptidases in vitro during protein purification procedures or in biological experiments involving cells or tissue culture. Typically, peptide chloromethyl ketone derivatives are used. However, these inactivators are quite nonspecific alkylating agents and experimental results can be misleading. For example, the presence of a chymotrypsin-like enzyme activity on the neutrophil membrane was assumed when ***inhibition*** with Tos-Phe-CH2Cl resulted in ***inhibition*** of the so-called oxidative burst of these cells. However, it has been shown that the targeted protein is not a serine peptidase, and ***inhibition*** results from a nonspecific alkylation reaction. As another example of the utility of phosphonates, dipeptide derivatives of .alpha.-aminoalkyl phosphonate diphenyl ester derivatives with a P1 proline residue are effective ***inhibitors*** for ***dipeptidyl*** - ***peptidase*** ***IV*** . The corresponding dipeptide boronic acid and chloromethyl ketone derivatives are ***unstable*** . In summary, peptidyl derivatives of .alpha.-aminoalkyl phosphonate diphenyl esters are highly specific irreversible ***inhibitors*** of serine peptidases and are chemically stable and stable in plasma. They offer a number of advantages over other types of ***inhibitors*** currently in use in biological experiments. After reaction with the enzyme, they form very stable enzyme- ***inhibitor*** complexes, making them interesting tools for X-ray studies on the active site structure of new serine peptidases.

=> d his

(FILE 'HOME' ENTERED AT 12:15:44 ON 16 JUL 2003)

```
     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA'   TERED AT
     12:16:08 ON 16 JUL 2003
L1          6267 S (DP IV) OR (DIPEPTIDYL PEPTIDASE IV)
L2             0 S L1 (P) INHIBT?
L3          1882 S L1 (P) INHIBIT?
L4             2 S L3 (P) MASKED
L5             1 DUPLICATE REMOVE L4 (1 DUPLICATE REMOVED)
L6            12 S L3 (P) UNSTABLE
L7             4 DUPLICATE REMOVE L6 (8 DUPLICATES REMOVED)

=> s (dipeptid? alkyl ketone) or (dipeptid? chloroalkyl ketone) or (dipeptid? cyanide)
L8             1 (DIPEPTID? ALKYL KETONE) OR (DIPEPTID? CHLOROALKYL KETONE) OR
                 (DIPEPTID? CYANIDE)

=> d l8 1 ibib abs

L8   ANSWER 1 OF 1  SCISEARCH  COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER:    78:95513  SCISEARCH
THE GENUINE ARTICLE: EP971
TITLE:               STERIC EFFECTS ON REACTION OF TRIETHYLENETETRAMINE WITH
                     NICKEL(II)-  ***DIPEPTIDEAMIDE***  -  ***CYANIDE***
                     COMPLEXES
AUTHOR:              PAGENKOPF G K (Reprint); MARCHESE W A
CORPORATE SOURCE:    MONTANA STATE UNIV, DEPT CHEM, BOZEMAN, MT, 59715
                     (Reprint)
COUNTRY OF AUTHOR:   USA
SOURCE:              JOURNAL OF COORDINATION CHEMISTRY, (1978) Vol. 7, No. 4,
                     pp. 249-252.
DOCUMENT TYPE:       Article; Journal
FILE SEGMENT:        PHYS
LANGUAGE:            ENGLISH
REFERENCE COUNT:     17


=> d his

     (FILE 'HOME' ENTERED AT 12:15:44 ON 16 JUL 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     12:16:08 ON 16 JUL 2003
L1          6267 S (DP IV) OR (DIPEPTIDYL PEPTIDASE IV)
L2             0 S L1 (P) INHIBT?
L3          1882 S L1 (P) INHIBIT?
L4             2 S L3 (P) MASKED
L5             1 DUPLICATE REMOVE L4 (1 DUPLICATE REMOVED)
L6            12 S L3 (P) UNSTABLE
L7             4 DUPLICATE REMOVE L6 (8 DUPLICATES REMOVED)
L8             1 S (DIPEPTID? ALKYL KETONE) OR (DIPEPTID? CHLOROALKYL KETONE) OR

=> s (peptid? alkyl ketone) or (peptid? chloroalkyl ketone) or (peptid? cyanide)
L9            13 (PEPTID? ALKYL KETONE) OR (PEPTID? CHLOROALKYL KETONE) OR (PEPTI
                 D? CYANIDE)

=> s l9 (p) l3
L10            0 L9 (P) L3

=> s (metabolic disorder) or (glucose tolerance) or (diabetes mullitus) or neuropathy
L11       277517 (METABOLIC DISORDER) OR (GLUCOSE TOLERANCE) OR (DIABETES MULLITU
                 S) OR NEUROPATHY

=> s l11 (p) l3
L12          140 L11 (P) L3

=> s l12 (p) (masked or prodrug or unstable)
L13            6 L12 (P) (MASKED OR PRODRUG OR UNSTABLE)

=> duplicate remove l13
DUPLICATE PREFERENCE IS 'CAPLUS, BIOSIS, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L13
L14            6 DUPLICATE REMOVE L13 (0 DUPLICATES REMOVED)

=> d l14 1-6 ibib abs

L14  ANSWER 1 OF 6  CAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:          2003:334905  CAPLUS
```

DOCUMENT NUMBER: 138:338500
TITLE: Novel [redacted]eptidyl peptidase IV (DP-IV) [redacted]bitors as anti-diabetic agents
INVENTOR(S): Evans, David Michael; Tartar, Andre
PATENT ASSIGNEE(S): Ferring B.V., Neth.
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003035067 | A1 | 20030501 | WO 2002-GB4787 | 20021023 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2001-25446 A 20011023
OTHER SOURCE(S): MARPAT 138:338500
GI

/ Structure 2 in file .gra /

AB The invention relates to a series of ***prodrugs*** of ***inhibitors*** of ***DP*** - ***IV*** with improved properties. Claimed compds. I [X = S, CH2; R1 = H, CN; R2 = (oxa)(thia)alkyl substituted by carbamoyl, (thio)acylamino, sulfonylamino, or amino groups; R3 = H2NCHR13CO, H2NCHR14CONHCHR15CO, CR16:CR17COR18, or R19O2C, where R13-R15 are side chains of the proteinaceous amino acids, R16 is H, alkyl, or Ph, R17 is H or alkyl, R18 is H, alkyl, OH, alkoxy, or Ph; R19 is (un)substituted alkyl or phenyl] can be used for the treatment of impaired ***glucose*** ***tolerance*** and type II diabetes. Thus, (2S)-1-[N.alpha.-(1-acetoxyethoxycarbonyl)-N.omega.-(pyrazinyl-2-carbonyl)-L-ornithinyl]pyrrolidine-2-carbonitrile was prepd. via coupling of (2S)-pyrrolidine-2-carbonitrile (prepn. given) with N.alpha.-tert-butoxycarbonyl-N.omega.-(pyrazinyl-2-carbonyl)-L-ornithine, followed by deprotection and acylation with .alpha.-acetoxyethyl p-nitrophenyl carbonate.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 6 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 2000:576230 SCISEARCH
THE GENUINE ARTICLE: 313NK
TITLE: ***Prodrugs*** of ***DP*** ***IV*** ***inhibitors*** strongly improve incretin-mediated ***glucose*** ***tolerance***
AUTHOR: Demuth H U (Reprint); Freyse E J; Berg S; Heinke P; McIntosh C C H; Pederson R A
SOURCE: DIABETES, (MAY 2000) Vol. 49, Supp. [1], pp. 944-944. Publisher: AMER DIABETES ASSOC, 1660 DUKE ST, ALEXANDRIA, VA 22314. ISSN: 0012-1797.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 0

L14 ANSWER 3 OF 6 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:2379 BIOSIS
DOCUMENT NUMBER: PREV200100002379
TITLE: ***Prodrugs*** of ***DP*** ***IV*** - ***inhibitors*** strongly improve incretin-mediated ***glucose*** ***tolerance*** .
AUTHOR(S): Demuth, Hans-Ulrich (1); Hoffmann, Torsten; Freyse, Ernst-Joachim; Berg, Sabine; Heinke, Peter; McIntosh,

Christopher H. S.; Pederson, Raymond A.
CORPORATE SOURCE: (1) Probiodrug Research GmbH, Halle/Saale Germany
SOURCE: Diabetes Research and Clinical Practice, (September, 2000) Vol. 50, No. Suppl. 1, pp. S386. print.
Meeting Info.: 17th International Diabetes Federation Congress on Diabetes Research and Clinical Practice Mexico-City, Mexico November 05-10, 2000
ISSN: 0168-8227.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L14 ANSWER 4 OF 6 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:504563 BIOSIS
DOCUMENT NUMBER: PREV200000504563
TITLE: ***Prodrugs*** of ***DP*** ***IV*** - ***inhibitors*** strongly improve incretin-mediated ***glucose*** ***tolerance*** .
AUTHOR(S): Demuth, Hans-Ulrich (1); Hoffmann, Torsten (1); Glund, Konrad (1); Freyse, Ernst-Joachim (1); Berg, Sabine (1); Heinke, Peter (1); McIntosh, Christopher H. S. (1); Pederson, Raymond A. (1)
CORPORATE SOURCE: (1) Probiodrug Research GmbH, Halle Germany
SOURCE: Regulatory Peptides, (25 October, 2000) Vol. 94, No. 1-3, pp. 59. print.
Meeting Info.: 13th International Symposium on Regulatory Peptides Cairns, Queensland, Australia October 22-26, 2000
ISSN: 0167-0115.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L14 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:819402 CAPLUS
DOCUMENT NUMBER: 132:36038
TITLE: Synthesis of prodrugs of unstable dipeptidyl peptidase IV inhibitors for use in treating diabetes
INVENTOR(S): Demuth, Hans-Ulrich; Schmidt, Jorn; Hoffmann, Torsten; Glund, Konrad
PATENT ASSIGNEE(S): Probiodrug Gesellschaft Fur Arzneimittelforschung m.b.H., Germany
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9967279 | A1 | 19991229 | WO 1999-EP4381 | 19990624 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| DE 19828114 | A1 | 20000127 | DE 1998-19828114 | 19980624 |
| CA 2335978 | AA | 19991229 | CA 1999-2335978 | 19990624 |
| AU 9947772 | A1 | 20000110 | AU 1999-47772 | 19990624 |
| AU 758843 | B2 | 20030403 | | |
| BR 9911415 | A | 20010320 | BR 1999-11415 | 19990624 |
| EP 1090030 | A1 | 20010411 | EP 1999-931163 | 19990624 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2002518518 | T2 | 20020625 | JP 2000-555930 | 19990624 |
| NO 2000006483 | A | 20001219 | NO 2000-6483 | 20001219 |
| US 2001020006 | A1 | 20010906 | US 2000-745883 | 20001221 |

PRIORITY APPLN. INFO.: DE 1998-19828114 A 19980624
WO 1999-EP4381 W 19990624

OTHER SOURCE(S): MARPAT 132:36038
GI

/ Structure 3 in file .gra /

AB The invention relates to compds. of ***unstable*** ***inhibitors*** of ***dipeptidyl*** ***peptidase*** ***IV*** ( ***DP*** ***IV*** ) which comprise general formula A-B-C, whereby A represents an amino acid, B represents the chem. bond between A and C or an amino acid, and C represents an ***unstable*** ***inhibitor*** of ***DP*** ***IV*** . Such compds. are used for treating altered ***glucose*** ***tolerance*** , glucosuria, hyperlipidemia, metabolic acidosis, diabetes mellitus, diabetic ***neuropathy*** , nephropathy, and secondary diseases in mammals caused by diabetes mellitus. Thus, (I) was reacted with pyridine to give [(II); R = Cbz], which was deprotected to give II (R = H)(III) which is thought to undergo an intramol. cyclization (no data) to form the active ***DP*** ***IV*** ***inhibitor*** . In 0.1 M HEPES-buffer, pH 7.6, at 25.degree., III had a half life (before self-cyclization) of 13.3 min.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:819401 CAPLUS

DOCUMENT NUMBER: 132:36037

TITLE: Synthesis and use of prodrugs of dipeptidyl peptidase IV inhibitors

INVENTOR(S): Demuth, Hans-Ulrich; Hoffmann, Torsten; Schlenzig, Dagmar; Manhart, Susanne

PATENT ASSIGNEE(S): Probiodrug Gesellschaft fur Arzneimittelforschung m.b.H., Germany

SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9967278 | A1 | 19991229 | WO 1999-EP4382 | 19990624 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| DE 19828113 | A1 | 20000105 | DE 1998-19828113 | 19980624 |
| CA 2335992 | AA | 19991229 | CA 1999-2335992 | 19990624 |
| AU 9949007 | A1 | 20000110 | AU 1999-49007 | 19990624 |
| BR 9911468 | A | 20010320 | BR 1999-11468 | 19990624 |
| EP 1087991 | A1 | 20010404 | EP 1999-932721 | 19990624 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| NO 2000006484 | A | 20001219 | NO 2000-6484 | 20001219 |
| US 2002049164 | A1 | 20020425 | US 2000-745776 | 20001222 |

PRIORITY APPLN. INFO.: DE 1998-19828113 A 19980624
WO 1999-EP4382 W 19990624

OTHER SOURCE(S): MARPAT 132:36037

AB The invention relates to ***prodrug*** compds. of ***inhibitors*** of ***dipeptidyl*** ***peptidase*** ***IV*** ( ***DP*** ***IV*** ). Said ***prodrug*** compds. comprise general formulas (A-B-C), whereby A represents an amino acid, B represents the chem. bond between A and C or an amino acid, and C represents a stabile ***inhibitor*** of ***DP*** ***IV*** . Such ***prodrug*** compds. are used for treating altered ***glucose*** ***tolerance*** , glucosuria, hyperlipidemia, metabolic acidosis, diabetes mellitus, diabetic ***neuropathy*** , nephropathy, and secondary diseases in mammals caused by diabetes mellitus. Thus, Boc-Pro-Ile-OH was coupled with thiazolidine, N-deprotected, reacted with Boc-Gy-OH, and then N-deprotected to give H-Gly-Pro-Ile-R (R = thiazolidine) (I). In in vivo tests using Wister rats, H-Ile-R, I, and H-Pro-Ile-R gave blood glucose levels of 74.4, 57.1, and 56.1% (compared to control = 100%) at doses of 2.5.mu.M/300 g wt.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
=> d his

     (FILE 'HOME' ENTERED AT 12:15:44 ON 16 JUL 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     12:16:08 ON 16 JUL 2003
L1          6267 S (DP IV) OR (DIPEPTIDYL PEPTIDASE IV)
L2             0 S L1 (P) INHIBT?
L3          1882 S L1 (P) INHIBIT?
L4             2 S L3 (P) MASKED
L5             1 DUPLICATE REMOVE L4 (1 DUPLICATE REMOVED)
L6            12 S L3 (P) UNSTABLE
L7             4 DUPLICATE REMOVE L6 (8 DUPLICATES REMOVED)
L8             1 S (DIPEPTID? ALKYL KETONE) OR (DIPEPTID? CHLOROALKYL KETONE) OR
L9            13 S (PEPTID? ALKYL KETONE) OR (PEPTID? CHLOROALKYL KETONE) OR (PE
L10            0 S L9 (P) L3
L11       277517 S (METABOLIC DISORDER) OR (GLUCOSE TOLERANCE) OR (DIABETES MULL
L12          140 S L11 (P) L3
L13            6 S L12 (P) (MASKED OR PRODRUG OR UNSTABLE)
L14            6 DUPLICATE REMOVE L13 (0 DUPLICATES REMOVED)

=> log y
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                     107.34     107.55

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                         ENTRY    SESSION
CA SUBSCRIBER PRICE                                      -3.26      -3.26

STN INTERNATIONAL LOGOFF AT 12:30:07 ON 16 JUL 2003
```